REMARKS

This is in response to the office action mailed April 01, 2005. A Petition for a one month extension of time and check are being mailed.

Claims 2 to 17 and 19 to 30 are now in this application. Claim 30 was earlier amended to recite that the enzymes on the first and second enzyme-anchor complexes respectively are different from each other, previously inferred from the recitation in the claim that these enzymes perform different functions.

(I) Request to Withdraw Finality of Office Action

The office action mailed April 4, 2005 has been made final. It is submitted that the finality of the office action is not appropriate in the circumstances and should be withdrawn.

Substantive claim amendments were introduced in the Response After Final dated July 22, 2004. *These claims amendments were never entered or considered* and an Advisory Action issued September 13, 2004. A Request for Continued Examination (RCE) was filed on October 28, 2004 with a request that the amended claims filed July 22, 2004 be examined. This is the therefore the ***first examination*** of the claims as pending in this application and the office action should not have been made final. It is submitted that these claims would **not** have been finally rejected on the grounds and art of record, *a fact acknowledged by the Examiner in the Advisory Action.*

Please therefore withdraw the finality of this office action.

(II) The Rejections

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as

failing to comply with the written description requirement.

Claims 2 to 17 and 19 to 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

(A) Rejection of Claim 30

The Examiner rejects claim 30 because the specification does not with the written description requirement, but it is submitted that this rejection is not supported by the facts. There is ample description and numerous examples in the specification to support claim 30, as shown by the number and content of examples that support a position that specification does contain descriptions that support the claimed matter. As an introduction, however, a brief explanation of the function described in claim 30 might be in order.

Claim 30 embodies three functions: (i) enzymatic dismantling and destruction of the biofilm structure along with the debris that are created in the destruction process; (ii) enzymatic killing of bacteria through lysis of the bacterial cell wall; and (iii) retention or anchoring of the two required enzymes at or near the biofilm structure. Each of these functions is adequately described in the specification such that one skilled in the art would be able to practice the invention and carry out the invention without undue experimentation. The following specific examples support claim 30. In addition, they individually support other claims, as identified.

(i) Descriptions of the enzymatic dismantling and destruction of the biofilm structure can be found in the specification in the following paragraphs (starting page and line of paragraph

indicated):

Page 2, line 25: By reference, extensive description of the dismantling and destruction of the biofilm can be found in U.S. Patent Nos. 5,871,714 and 6,159,447. Consequently, the dismantling and destruction of a biofilm is not new. The present invention builds upon the previous invention in two ways: 1. destruction of the debris created when a biofilm is dismantled; and 2. the subsequent treatment of the bacteria that reside within the biofilm structure and become exposed during the process of biofilm dismantling and destruction.

Page 3, line 1: "... the viscosity of the sputum from cystic fibrosis patients was reduced when the sputum was treated with the enzyme DNase." This statement in the specification is supported by a scientific publication that not only supports the statement in the specification, but also describes the common and standard biochemical and biotechnological procedures of cloning, expression and characterization of synthesized enzymes. The purpose of citing the reference was to accomplish exactly what the examiner said was missing from the specification. (Also supports claims 6, 22, 24).

Page 4, line 6: "One aspect of the invention consists of one or more enzymes(s) whose specificity includes its (their) ability to degrade the polysaccharide backbone of the biofilm structure produced by *Pseudomonas aeruginosa* that occur in the respiratory tract of cystic fibrosis patients." (Also supports claim 2).

Page 7, line 9: "... one other enzyme is hydrolytic in

nature, having the capability to degrade extraneous byproducts of both the biofilm and host-originated materials." (Also supports claims 6).

Page 8, line 5: The example in this paragraph of the specification, "The enzymes capable of degrading proteins..." speaks to extraneous byproducts. The proteins, among other chemicals are the "other materials" associated with the biofilm identified at page 10, line 16.

Page 10, line 16: "... degradation and removal of the biofilm backbone structure along with any other materials that may be associated with the backbone, which collectively constitute the entire biofilm." (Also supports claims 2 and 6).

Page 15, line 28: "... enzyme-anchor complex having an enzyme that degrades the biofilm ...". (Also supports claim 2).

Page 17, line 29: "... enzymes in the class EC 4.2.2.-, which are polysaccharide lyases, which degrade the polysaccharide backbone structure of biofilms:" Listing of examples of polysaccharide degrading enzymes are seen in subsequent list. (Also supports claims 2 and 5).

Page 21, line 4: "... a wide variety of alginate lyase and polysaccharide depolymerase enzymes with degrade alginate by various mechanisms." (Also supports claims 2 and 5).

(ii) Description of the enzymatic killing and lysis of the bacteria can be found in the following paragraphs.

Page 10, line 27: "... the other enzyme(s) has (have) the capability of acting directly upon the bacteria, causing lysis of the bacterial cell wall." (Also supports claims 25, 26, 27, 28 and 29).

Page 11, line 14: "Lysozyme has long been known to have bactericidal activity by destroying the bacterial cell wall ...". (Also supports claims 25, 26, 27, 28 and 29).

Page 11, line 27: "... lysozyme can be anchored with elastase and used in conjunction with any one of the following biofilm-degrading enzymes: alginate lyase ...". (Also supports claims 5 and 26).

Page 12, line 10: "Examples of enzymes that have the capability to kill bacteria are as follows: Lysozyme ... bacteriophage polysaccharide depolymerase; Holin enzymes." (Also supports claims 25, 26, 27, 28 and 29).

(iii) Description of the retention or anchoring function which is applicable to both enzymes, those that dismantle/degrade the biofilm structure and those that act directly upon the bacteria and kill them, are found in the following paragraphs:

Page 4, line 19: "Attached to the enzyme(s) ... are one or more moieties that have the capability of binding ... Collectively, these moieties are called anchors." (Also supports claims 3, 4, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 and 21).

Page 5, line 9: "Moieties with a Known Affinity for Biofilms". (Also supports claims 7, 8, 9, 10, 11, 12, 13, 14, 15,

16, 17 and 21).

Page 17, line 18: "Types of Anchors. The binding domain from elastase ... Additional anchors listed in U . Patent No. 5,871,714." (Also supports claims 7, 8 and 21).

Extensive examples are given in the specification for two procedures for constructing enzyme-anchor complexes. These procedures for synthesizing the two distinct enzyme-anchor complexes are incorporated into the specification by reference and have not been listed as specific examples. Such references [Proc. Natl. Acad. Sci. 87, 9188-9192(1990) and U. S. Pat. No. 5,871,714], serve the purpose of examples of the two synthetic procedures, chemical and molecular biology/biotechnological techniques that can be employed. Because the synthetic procedures for constructing enzyme-anchor complexes, as well as other details regarding the present invention, are at the least incorporated into this specification by reference does not detract from the validity or completeness of the specification. (Also supports claims 3, 4, 6, 19 and 20).

Page 10, line 16: "Attached to the enzymes ... through chemical synthetic procedures or recombinant technology ...". (Also supports claims 3 and 4).

Page 10, line 27: "The moieties are attached to the enzymes, either through chemical synthetic procedures or recombinant technology ...". (Also supports claims 3 and 4).

Page 17, line 13: "The Anchor Enzyme Complex can be constructed using chemical synthetic techniques. Additionally, the

Anchor-Enzyme complex, if the anchor is a polypeptide or protein, such as protein binding domains, lectins, selectins, heparin binding domains etc., can be constructed using recombinant genetic engineering techniques.". (Also supports claims 3, 4 and 20).

Page 21, line 24: "... a fusion protein is created using standard genetic engineering techniques. ... The bifunctional protein fulfills the criteria ... the binding domain derived from elastase serves as the anchor and the alginate lyase portion of the fusion protein serves as the degradative enzyme for the biofilm.". (Also supports claims 3, 5, 7, 8, and 19).

Page 22, line 9: "Using molecular biology and biotechnology techniques, gene fusions are created to produce unique proteins from recombinant DNA segments. ... The resulting fused DNA segment will produce a unique protein that possesses both enzymatic or catalytic activity and binding activity."

(B) Rejection of Claims 2-17 and 19-30

The examiner also inappropriately rejects claims 2-17 and 19-30 as "failing to comply with the enablement requirement." He states that subject matter in the claims was not described in the specification in such a way as to enable one skilled in the art to make and use the invention. Applicant repeats and refers to the copious examples given above to rebut the rejection of claim 30, many of which are applicable in this context as well. Furthermore, every claim in the application is supported by examples in the specification.

The examiner cites eight specific factors that are used to assess whether or not a disclosure would require undue

experimentation. The examiner states that the specification for the cystic fibrosis fails to provide guidance that would allow the skilled in the art to practice the invention without resorting to undue experimentation.

(i) The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art.

The examiner states: "The relative skill of those in the art is generally that of a Ph.D. or M.D. The present invention or composition is unpredictable unless experimentation is shown for the actual combination of the two individual enzyme components."

Response:

The educational level for one practicing the art is clearly very high, and those persons would be assumed to have considerable knowledge and experience in this field of art. But the examiner ascribes no value to the experience and knowledge of such highly skilled people. Furthermore, the procedures outlined in the cited references, construction of recombinant proteins, enzyme assay procedure, incubations to grow bacteria and biofilms etc. are the types of experiments conducted in undergraduate biochemistry, molecular biology and microbiology laboratories, well below the level of skill of those acknowledged by the Examiner.

The examiner provides no basis for the objection that the composition is unpredictable. The inventors, however, provide adequate reference to the individual experimental procedures which are outlined in U.S. Patent Nos. 5,871,714 and 6,159,447 and in the scientific literature: Proc. Natl. Acad. Sci. 87, 9188-9192(1990) [PNAS 1990], Appl. Environ. Microbiol. 93(9), 3724-3728(1997) and

Proc. Natl. Acad. Sci. 98, 4107-4112(2001) [PNAS2001]. Furthermore, the experimental aspects of the invention requiring techniques that are not described in the cited references are laid out in the present specification on pages 23 to 25.

The construction of the enzyme-anchor complexes through a chemical synthesis is described in the cited patents. The construction of the enzyme-anchor complexes by recombinant techniques is common procedure, considered as general skill in the art and available in multiple texts and manuals, some used in undergraduate biochemistry laboratory manuals. In addition, the procedure for the recombinant synthesis is outlined in the 1990 PNAS article.

The concentrations of the enzyme-anchor complexes are described in the 1990 PNAS article, the 2001 PNAS article and the Applied and Environmental Microbiology article from 1997. All three references cited in the specification (and many others besides) demystify and contradict the Examiner's finding of "unpredictability" and "undue experimentation."

The assay procedure for assessing the biofilm degrading enzyme-anchor complex is described in the application from page 23, line 3. The assay procedure for assessing the bacterial lysing enzyme complex in the presence of biofilms is described in the same section. Additional procedures are available in the 2001 PNAS article, which is entitled, "Prevention and Elimination of Upper Respiratory Colonization of Mice by Group A Streptococci by Using a Bacteriophage Lytic Enzyme."

The cited references were incorporated into the application

for a purpose. These are references which could be read by one skilled in the art who may wish to practice this invention. Therefore, if the Examiner challenges the application on the basis of absence of descriptive material, this should only be done after reading the references to avoid unsupported rejections of the claims.

The present invention, with its attendant references, describes the two methods (chemical and recombinant) for synthesizing the enzyme-anchor complexes, the test system conditions, including concentrations, and the specific assay procedures for both functionalities of the composition: dismantling and destruction of the biofilm and bacterial cell lysing/killing capability. Following these procedures makes the invention quite predictable and practicing the invention will be no more ill defined or difficult than any other bacterial-related invention.

(ii) Breadth of the claims.

The Examiner states: "The claims are very broad and inclusive to all and any two individual enzyme-anchor complexes combined together into a single composition." It is submitted that this is not an accurate reflection of the contents of the application. The fact that the focus of the invention is a treatment for cystic fibrosis and that in and of itself is limiting and cannot, in anyway, include "all" or "any" enzyme-anchor complexes. There is also a dual functional limitation: limitation to the enzyme that will specifically dismantle and degrade the biofilm associated with cystic fibrosis and an inherent limitation to enzymes that cause bacterial cell lysis. Finally, while the same anchor may be used for both enzyme-anchor complexes, the anchor is limited to its ability to bind to a surface at or near the biofilm structure.

Contrary to the Examiner's opinion, the claims are restrictive and are the opposite of being "very broad". The Examiner fails to define "very broad" other than state "inclusive to all and any" which obviously cannot be the case based on the desired functional outcome of the composition in its focused application.

(iii) The amount of direction or guidance provided and the presence or absence of working examples.

The purpose of incorporating examples into a specification is to assist those skilled in the art to practice the invention. Assistance to those skilled in the art to practice the invention can be accomplished in other ways e.g. references to prior art, scientific literature, graphics etc. The present invention cites prior art and scientific literature. In addition, the specification contains descriptive drawings to assist one skilled in the art to practice the invention. The present invention does contain analytical procedures to assess the dual function of simultaneous biofilm removal and bacterial lysis/kill, which is not described in prior art or in the scientific literature. The examples, which are diverse analyses, are required to fully implement the present invention and consequently, Applicant included these procedures because they were necessary to fully implement the invention.

(iv) The quantity of experimentation necessary.

The statement by the examiner that the "level of experimentation needed to determine the combination of two individual enzyme-anchor complexes into a single composition is undue" is not quantifiable, unsubstantiated and inaccurate. Anyone skilled in the art (and the level of skill is high), using the cited scientific literature and standard biochemistry texts, undergraduate laboratory manual or commonly used reference volumes

such as Methods in Enzymology, would be readily able to select the appropriate amount of enzyme necessary to lyse/kill bacteria. Anyone skilled in the art, using the cited scientific references in conjunction with the disclosed invention, could readily select the appropriate amount of enzyme-anchor complex, based on the published enzymatic activity required to dismantle and destroy the cystic fibrosis biofilm.

The Examiner appears to assume some relationship, stoichiometrically or otherwise, between the two enzyme-anchor complex for their respective functionality. No relationship between the diverse functions of the enzyme-anchor complexes is stated or implied in the specification. Consequently, the need for specific compositional examples does not exist and the absence of compositional examples will not require "undue" experimentation. The only burden for implementation upon the inventors is that adequate direction be given so that the invention can be practiced by on skilled in the art. The present invention fulfills that requirement.

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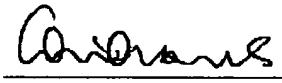
Based on the exhaustive discussion above addressing the Examiner's findings, favorable reconsideration of the claims and allowance of the application is respectfully requested.

Respectfully submitted,



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Enclosed: Petition for extension and check (by mail)

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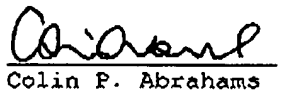

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